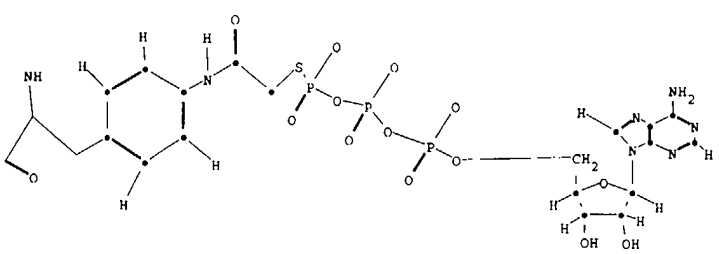
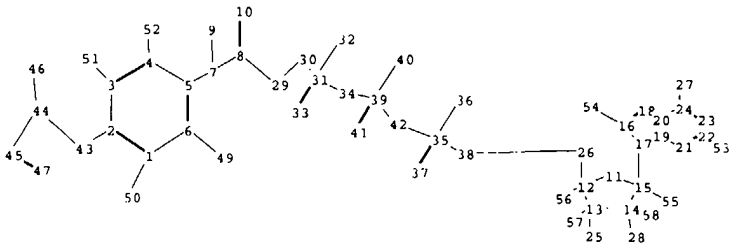
09/811,870 SEARCH STRATEGY

```
     (FILE 'HOME' ENTERED AT 15:35:32 ON 13 NOV 2003)

     FILE 'CAPLUS' ENTERED AT 15:35:40 ON 13 NOV 2003
                E COLE P A/AU 25
L1           10 S (E3 OR E48 OR E49 OR E50 OR E51 OR E54) AND (KINASE AND INHIB
                E PARANG K/AU 25
L2            4 S (E3 OR E4 OR E5) AND (KINASE AND INHIBITOR)
                E ABLOOGU A/AU 25
L3            4 S (E1 OR E2 OR E4) AND (KINASE AND INHIBITOR)
                E KOHANSKI R A/AU 25
L4            7 S (E3 OR E4 OR E5 OR E6 OR E7) AND (KINASE AND INHIBITOR)
                E COURTNEY A/AU 25
L5            1 S (E3 OR E5 OR E11 OR E12) AND (KINASE AND INHIBITOR)

     FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT
     15:40:05 ON 13 NOV 2003
L6          105 S BISUBSTRATE (W) INHIBITOR
L7           54 S L6 AND (KINASE)
L8           19 DUP REM L7 (35 DUPLICATES REMOVED)

=>
```

	Type	L #	Hits	Search Text	DBs	Time Stamp
1	BRS	L1	2	5990094.pn.	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:28
2	BRS	L2	6944	cole.in. or parang.in. or abloogu.in. or kohanski.in. or courtney.in.	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:28
3	BRS	L3	20	l2 and ((bisubstrate or inhibitor) and kinase)	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:33
4	BRS	L4	10	bisubstrate adj inhibitor	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:33
5	BRS	L5	8	l4 and kinase	USPAT; US-PGP UB; EPO; JPO; DERWE	2003/11/13 15:33

C:\Program Files\Stnexp\Queries\compound2.str





chain nodes :
7 8 9 10 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44
45 46 47 49 50 51 52 53 54 55 56 57 58
ring nodes :
1 2 3 4 5 6 11 12 13 14 15 16 17 18 19 20 21 22 23 24
chain bonds :
1-50 2-43 3-51 4-52 5-7 6-49 7-8 7-9 8-10 8-29 12-26 12-56 13-25 13-57 14-28
14-58 15-17 15-55 16-54 22-53 24-27 26-38 29-30 30-31 31-32 31-33 31-34 34-39
35-38 35-36 35-37 35-42 39-41 39-40 39-42 43-44 44-45 44-46 45-47
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-15 12-13 13-14 14-15 16-17 16-18 17-19 18-20
19-20 19-21 20-24 21-22 22-23 23-24
exact/norm bonds :
5-7 7-8 8-10 11-12 11-15 12-13 13-14 13-25 14-15 14-28 15-17 16-17 16-18 17-19
18-20 24-27 29-30 30-31 31-32 31-33 31-34 34-39 35-38 35-36 35-37 35-42 39-41
39-40 39-42 44-46 45-47
exact bonds :
1-50 2-43 3-51 4-52 6-49 7-9 8-29 12-26 12-56 13-57 14-58 15-55 16-54 22-53
26-38 43-44 44-45
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 19-20 19-21 20-24 21-22 22-23 23-24
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS
31:CLASS 32:CLASS 33:CLASS 34:Atom 35:CLASS 36:CLASS 37:CLASS 38:Atom 39:CLASS
40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 49:CLASS
50:CLASS 51:CLASS 52:CLASS 53:CLASS 54:CLASS 55:CLASS 56:CLASS 57:CLASS 58:CLASS

09/891865 SEARCH STRATEGY

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PASSWORD:
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NEWS	3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS	4	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	5	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	6	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	7	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	8	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS	9	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS	10	SEP 22	DIPPR file reloaded
NEWS	11	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS	12	SEP 29	DISSABS now available on STN
NEWS	13	OCT 10	PCTFULL: Two new display fields added
NEWS	14	OCT 21	BIOSIS file reloaded and enhanced
NEWS	15	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced

NEWS EXPRESS	OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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FILE 'HOME' ENTERED AT 13:11:16 ON 13 NOV 2003

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:11:27 ON 13 NOV 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 NOV 2003 HIGHEST RN 616193-58-9
DICTIONARY FILE UPDATES: 12 NOV 2003 HIGHEST RN 616193-58-9

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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09/891865 SEARCH STRATEGY

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading compound2.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 13:12:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 13:12:32 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L3 1 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 148.55 148.76

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FILE COVERS 1907 - 13 Nov 2003 VOL 139 ISS 20
FILE LAST UPDATED: 12 Nov 2003 (20031112/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 2 L3

=> d l- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:713377 CAPLUS

09/891865 SEARCH STRATEGY

DOCUMENT NUMBER: 135:253738
TITLE: Bisubstrate inhibitors of kinases
INVENTOR(S): Courtney, Aliya; Cole, Philip A.; Parang, Keykavous; Abloogu, Ararat; Kohanski, Ron
PATENT ASSIGNEE(S): Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070770	A2	20010927	WO 2001-US8886	20010321
WO 2001070770	A3	20020704		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002031820	A1	20020314	US 2001-811870	20010321

PRIORITY APPLN. INFO.: US 2000-190799P P 20000321

AB Protein kinase inhibitors have applications as anti-cancer therapeutic agents and biol. tools in cell signalling. Potent and selective bisubstrate inhibitors for the insulin receptor tyrosine kinase are based on a phosphoryl transfer mechanism involving a dissociative transition state. One such inhibitor is synthesized by linking ATP.gamma.S to a peptide substrate analog via a two-carbon spacer. The compd. is a high-affinity competitive inhibitor against both nucleotide and peptide substrate and shows a slow off-rate. A crystal structure of this inhibitor bound to the tyrosine kinase domain of the insulin receptor confirms the key design features inspired by a dissociative transition state, and reveal that the linker takes part in the octahedral coordination of an active site Mg2+ ion. A Kemptide-ATP.gamma.S compd. was also prepd. This compd. was an inhibitor of protein kinase A.

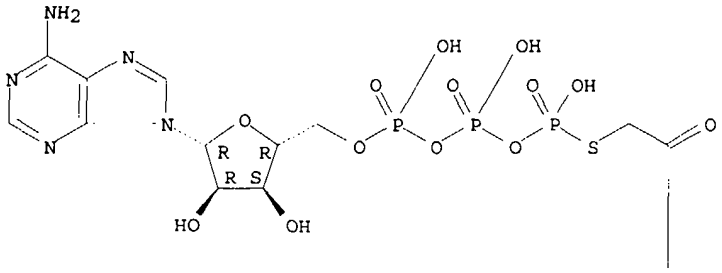
IT **329783-44-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(insulin receptor tyrosine kinase inhibitor; bisubstrate inhibitors of kinases)

RN 329783-44-0 CAPLUS

CN L-Aspartic acid, N2-acetyl-L-lysyl-L-lysyl-L-lysyl-L-leucyl-L-prolyl-L-alanyl-L-threonylglycyl-L-.alpha.-asparty1-4-[[6-(5'-adenylyloxy)-4,6-dihydroxy-4,6-dioxido-1-oxo-5-oxa-3-thia-4,6-diphosphahex-1-yl]amino]-L-phenylalanyl-L-methionyl-L-asparaginyl-L-methionyl-L-seryl-L-prolyl-L-valylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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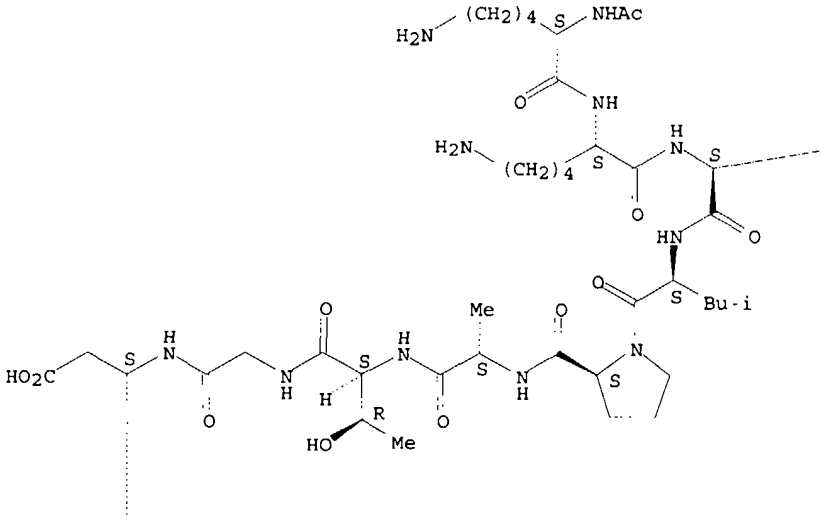

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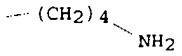

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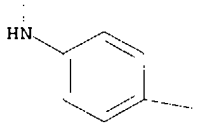

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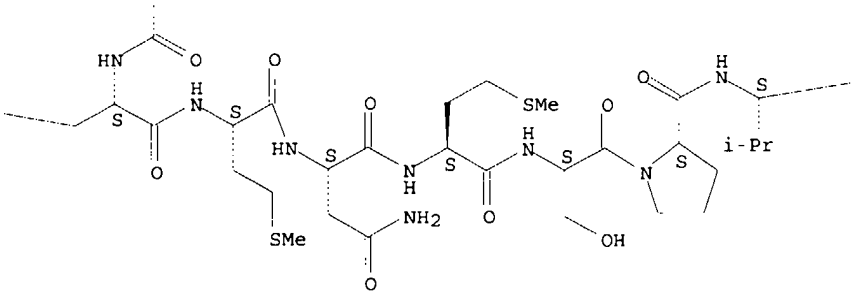

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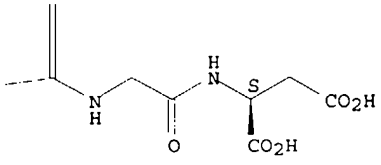


L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:37882 CAPLUS
DOCUMENT NUMBER: 134:218831
TITLE: Mechanism-based design of a protein kinase inhibitor
AUTHOR(S): Parang, Keykavous; Till, Jeffrey H.; Ablooglu, Ararat J.; Kohanski, Ronald A.; Hubbard, Stevan R.; Cole, Philip A.
CORPORATE SOURCE: Department of Pharmacology and Molecular Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA

09/891865 SEARCH STRATEGY

SOURCE: Nature Structural Biology (2001), 8(1), 37-41
CODEN: NSBIEW; ISSN: 1072-8368
PUBLISHER: Nature America Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

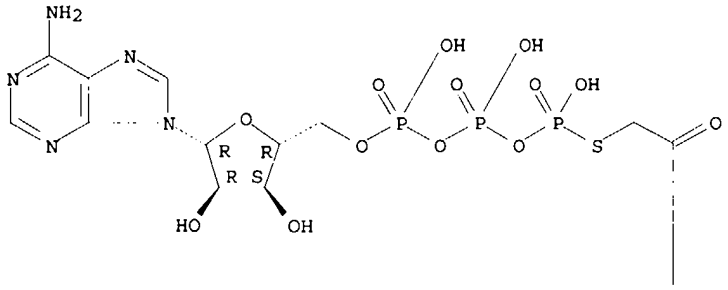
AB Protein kinase inhibitors have applications as anticancer therapeutic agents and biol. tools in cell signaling. Based on a phosphoryl transfer mechanism involving a dissociative transition state, a potent and selective bisubstrate inhibitor for the insulin receptor tyrosine kinase was synthesized by linking ATP.gamma.S to a peptide substrate analog via a two-carbon spacer. The compd. was a high affinity competitive inhibitor against both nucleotide and peptide substrates and showed a slow off-rate. A crystal structure of this inhibitor bound to the tyrosine kinase domain of the insulin receptor confirmed the key design features inspired by a dissociative transition state, and revealed that the linker takes part in the octahedral coordination of an active site Mg2+. These studies suggest a general strategy for the development of selective protein kinase inhibitors.

IT **329783-44-0D**, complexes with insulin receptor kinase
RL: PRP (Properties)
(crystal structure of bisubstrate inhibitor complexes with insulin receptor kinase)

RN 329783-44-0 CAPLUS

CN L-Aspartic acid, N2-acetyl-L-lysyl-L-lysyl-L-lysyl-L-leucyl-L-prolyl-L-alanyl-L-threonylglycyl-L-.alpha.-aspartyl-4-[[6-(5'-adenylyloxy)-4,6-dihydroxy-4,6-dioxido-1-oxo-5-oxa-3-thia-4,6-diphosphahex-1-yl]amino]-L-phenylalanyl-L-methionyl-L-asparaginyl-L-methionyl-L-seryl-L-prolyl-L-valylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/891865 SEARCH STRATEGY

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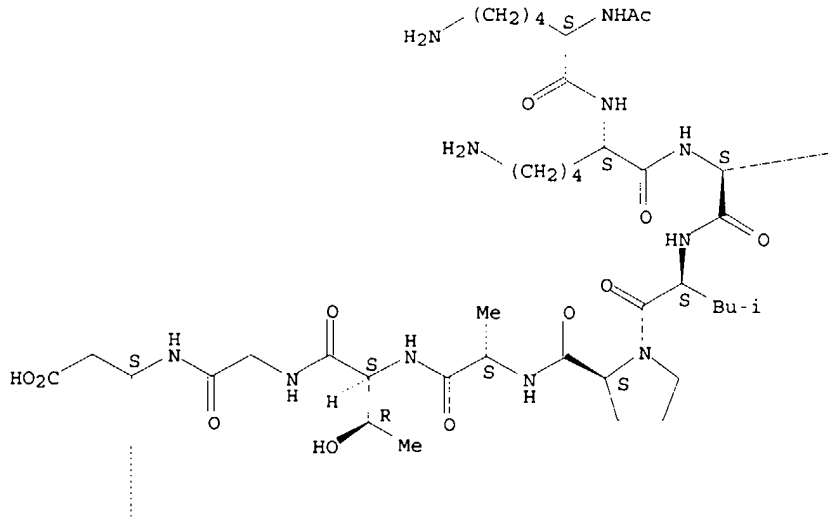

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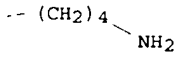

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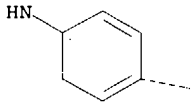

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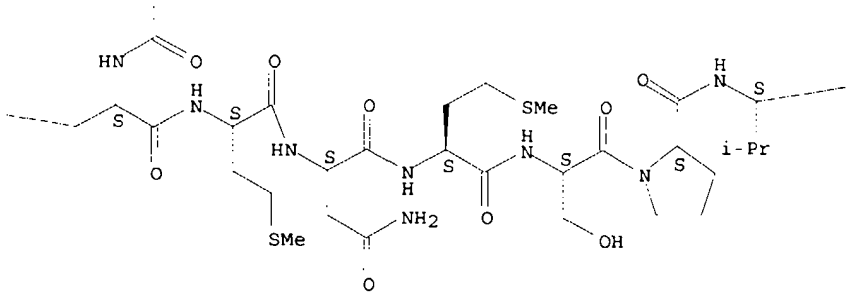

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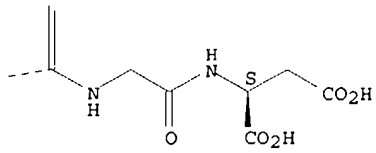

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(mechanism-based design of bisubstrate inhibitor of insulin receptor kinase

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.49	158.25

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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